

THE AMENDMENTSIn the Specification

At page 4, amend the paragraph starting at line 20:

where the sum of m+n+p is from [[1]] 0 to 5;

At page 4, amend the paragraph starting at line 23:

B' is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the [[5']] 1' position of the furanose or carbocycle via the 9- or 1- position, respectively;

At page 6, amend the paragraph starting at line 17:

where the sum of m+n+p is from [[1]] 0 to 5;

At page 6, amend the paragraph starting at line 20:

B' is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the [[5']] 1' position of the furanose or carbocycle via the 9- or 1- position, respectively;

At page 8, amend the paragraph starting at line 7:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

Z= OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II;

At page 8, amend the paragraph starting at line 17:

such that the sum of m+n+p is from [[1]] 0 to 5;

At page 8, amend the paragraph starting at line 20:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III;

At page 9, amend the paragraph starting at line 5:

such that the sum of m+n+p is from [[1]] 0 to 5;

At page 9, amend the paragraph starting at line 10:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

Z= OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II;

At page 9, amend the paragraph starting at line 25:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III;

At page 10, amend the paragraph starting at line 9:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

Z= OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II;

At page 10, amend the paragraph starting at line 23:

M= H, NH₄⁺ NH₄[±], Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III;

At page 11, amend the paragraph starting at line 13:

M= H, NH₄⁺ NH₄[±], Na Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

At page 11, amend the paragraph starting at line 19:

n and p = 0,1, 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or

At page 11, amend the paragraph starting at line 25:

M= H, NH₄⁺ NH₄[±], Na Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= OR₁, where OR₁ falls under the definition of general formula III;

Z'= OR₂, where OR₂ falls under the definition of general formula III;

At page 12, amend the paragraph starting at line 5:

n and p = 0,1, 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or

At page 12, amend the paragraph starting at line 11:

M= H, NH₄ NH₄[±], Na Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

At page 12, amend the paragraph starting at line 24:

M= H, NH₄⁺ NH₄[±], Na+ Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= OR₁, where OR₁ falls under the definition of general formula III;

Z'= OR₂, where OR₂ falls under the definition of general formula III;

At page 13, amend the paragraph starting at line 5:

M= H, NH₄ NH₄⁺, Na Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'=H, OH or OR₂, where OR₂ falls under the definition of general formula II;

At page 13, amend the paragraph starting at line 19:

M= H, NH₄ NH₄⁺, Na Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

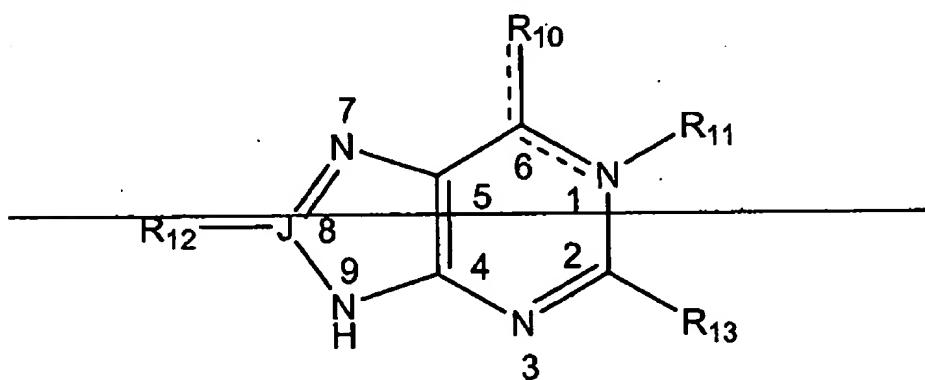
Z'= H, OH or OR₂, where OR₂ falls under the definition of general formula III;

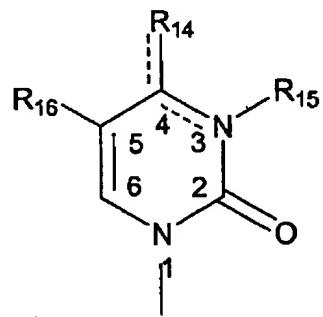
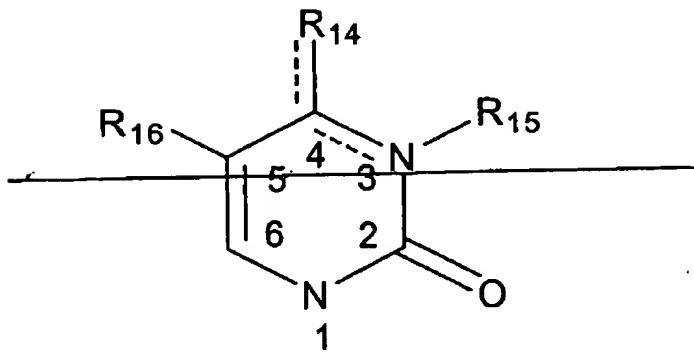
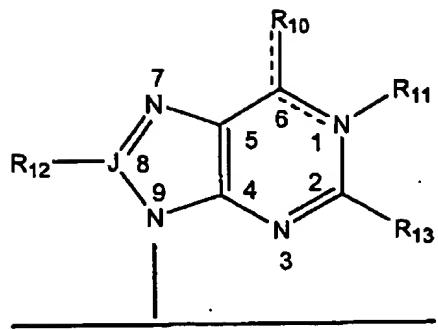
At page 15, amend the paragraph starting at line 10:

and [[R9]] R₉ is alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy.

At page 16, amend the chemical structures:

Formula IV





Amend the paragraph starting at page 18, line 15:

The compounds of the present invention may be prepared by derivatization or substitution at the level of the nucleoside, followed by phosphorylation and condensation as previously described, or the reactions may be carried out directly on the preformed mono- or dinucleotides. In the general formulas

Ia and Ib, the substituents at Y', Z', Y, and Z may be esters, carbamates, or carbonates, which are generally described by formula II. Esters may be readily prepared by reacting a hydroxyl group of the furanose in a nucleoside or nucleotide with an activated form of an appropriate organic acid, such as an acid halide or acid ~~anyhydride~~ anhydride in the presence of an organic or inorganic base. Alternately, use of a suitable coupling reagent such as dicyclohexylcarbodiimide, 1,1'-carbonyldiimidazole and the like to activate the organic acid may be used to achieve the same result.

Amend the paragraph starting at page 19, line 12:

Cyclical orthoesters may be prepared by reaction of the neighboring 2' and 3' hydroxyl groups of a furanose with an ~~acyclic~~ acyclic orthoester, in the presence of an acid. When the nucleoside or nucleotide to be derivatized is a purine that contains a 6-amino functionality or is a pyrimidine that contains a 4-amino functionality, it may be converted to the respective urea or thiourea by treatment with isocyanates or isothiocyanates, respectively, as was previously described for carbamates or thiocarbamates of the 2' or 3' hydroxyls of the furanose. It was found that reactions of the amino group with isocyanates or isothiocyanates could be carried out in the presence of the hydroxyl groups of the furanose, by appropriate manipulation of the stoichiometry of the reaction.

Amend the two paragraphs starting at page 29, line 10:

The active compounds may be administered systemically to target sites in a subject in need such that the extracellular concentration of a P2Y_T agonist antagonist is elevated to block the binding of ADP to P2Y_T receptors, thus inhibit the platelet aggregation. The term systemic as used herein includes subcutaneous injection, intravenous, intramuscular, intrasternal injection, intravitreal injection, infusion, inhalation, transdermal administration, oral administration, rectal administration and intra-operative instillation.

For systemic administration such as injection and infusion, the pharmaceutical formulation is prepared in a sterile medium. The active ingredient, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Adjuvants such as local anesthetics, preservatives and buffering agents can also be dissolved in the vehicle. The sterile indictable preparation may be a sterile indictable solution or suspension in a non-toxic acceptable diluent or solvent. Among the acceptable vehicles and solvents that may be employed are sterile water, saline solution, or Ringer's solution.